Case Reports

Intravenous Marijuana Syndrome

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THE INTRAVENOUS (IV) INJECTION of boiled marijuana broth causes a distinct clinical syndrome. To date, 24 cases of this syndrome have been reported in the English language literature.[1-9] We report the 25th case and review the literature.

Report of a Case

In mid-January 1983, a 26-year-old man was evaluated at Providence Medical Center (Portland) for fever, myalgias, nausea and vomiting. He had boiled marijuana, strained the broth through cotton and injected it into his antecubital vein. One hour later, he had cough, nausea, vomiting, diarrhea, pain in his back and legs and fever. These symptoms persisted, and after 3½ hours he came to the emergency room. He had injected marijuana once previously and experienced pleasant psychological effects only. He had occasionally used LSD, cocaine and hydromorphone hydrochloride (Dilaudid) by nonintravenous routes, but denied other recent drug use. His past history was otherwise unremarkable. On physical examination he had a blood pressure of 60/40 mm of mercury, a heart rate of 110, a temperature by mouth of 40.8°C (105.4°F) and tender, weak arm musculature.

Initial laboratory studies elicited the following values: hematocrit 43.8%; leukocyte count 6,000 per μl, of which 69% were polymorphonuclear leukocytes and 23% bands; platelet count 209,000 per μl; creatinine 1.8 mg per dl; blood urea nitrogen (BUN) 17 mg per dl; potassium 3.6 mEq per liter; phosphate 1.5 mg per dl; asparate aminotransferase 28 IU per liter; lactic dehydrogenase 259 IU per liter, and creatine kinase (CK) 236 IU per liter. Urinalysis showed 30 mg per dl of protein. The chest x-ray film and electrocardiogram were normal. The arterial pH was 7.41.

The patient was admitted, given normal saline intravenously and treated empirically with a regimen of nafcillin sodium and tobramycin. Over the first 24 hours he received six liters of fluid and had a urine output of four liters. Despite a blood pressure of 70/50 mm of mercury, the central venous pressure measured 12 cm of water. Administration of dopamine hydrochloride was begun. On the evening of admission the leukocyte count fell to 1,500 per μl and the phosphate level to 0.5 mg per dl. By day 2 he had become afebrile and his blood pressure had risen to 100/70 mm of mercury on a regimen of 11 μg per kg per minute of dopamine. Repeat CK level measured 2,340 IU per liter, 2.7% of which was of the MB fraction; a serum myoglobin level was 435 ng per ml (normal 6 to 83), urine myoglobin 1,950 ng per ml, serum creatinine 2.4 mg per dl and serum phosphate 2.1 mg per dl. On day 3 his blood pressure was 100/60 mm of mercury off dopamine therapy, leukocyte count 26,000 per μl and platelet count 93,000 per μl. Cultures were negative after 48 hours and antibiotic therapy was discontinued. On day 5 he was discharged. One week later the serum creatinine level had fallen to 1.4 mg per dl, the CK level to 70 IU per liter and all symptoms had resolved.

Discussion

In 1968 Henderson and Pugsley first described the syndrome of emesis, myalgia and hypotension following the IV injection of broth derived from boiled marijuana.[1] In the present report we describe the 25th case of this syndrome. There have been 16 additional reports of such cases in sufficient detail to allow a review of clinical and laboratory features (Table 1). We have assumed that a feature was absent if not noted by the author; thus, the percentages in the table represent minimum figures. Symptoms began within a half hour in 14 and within an hour in all 17 cases. Initial symptoms included myalgia, nausea and vomiting, diarrhea, abdominal pain and weakness. Presenting signs involved tachycardia, hypotension, fever, tachypnea, muscle tenderness and hepatomegaly. Muscle weakness was not clearly shown. Of interest is that 15 patients had a normal mental state. All patients required IV administration of fluid and five required vasopressors for maintaining blood pressure. All 25 patients survived; the mean reported hospital stay was 9.1 days.

Several laboratory findings are noteworthy (Table 1). Leukocyte counts ranged from 1,100 to 41,000 per μl. Of 17 patients, 14 had pronounced leukocytosis of greater than 20,000 per μl,[1,2,4,6-9] while three manifested early leukopenia.[2,3] Platelet counts were less than 100,000 per μl in eight patients.[1,2,6,7,9] Azotemia was present in 14, with a mean BUN level of 75 mg per dl and a mean creatinine value of 5.8 mg per dl for 8 patients for whom a value was reported.[1-3,6-9] In six cases, an elevated bilirubin level (mean 4.1 mg per dl for ten patients)[1-3,6,7,9] or a CK level[2,7,9] or a pulmonary abnormality[1-3,7,9] was noted.

The pathophysiology of this syndrome remains unclear. While hypotension may be partially due to hypovolemia resulting from diarrhea and emesis, evidence of vasodilation has been noted clinically and may be the major mechanism.[9] While sepsis has been considered, bacteremia has not been found, though circulating endotoxin has not been excluded as a possible mechanism. In a study in which normal subjects were given cannabinoids intravenously, the components of marijuana responsible for more typical somatic and psychological changes, neither hypotension nor other adverse effects described above were induced.[10] Similarly, our patient had no apparent toxicity from a previous marijuana injection. Because the specific composition of the material injected by the

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ABBREVIATIONS USED IN TEXT

BUN = blood urea nitrogen
CK = creatine kinase
DIC = disseminated intravascular coagulation
IV = intravenous

25 patients is unknown, it is possible that the dose exceeded that given the normal experimental subjects or that a contaminant may have been responsible for the somatic toxicity. In at least seven cases, cotton was used to strain the broth before injecting.[2,3,7,8] "Cotton fever" has been reported following the IV use of heroin reclaimed from previously used cotton filters[11] and consists of emesis, myalgia and fever; thus, it partially resembles the IV marijuana syndrome.

The combination of diffuse myalgia and an elevated unfractionated serum CK level suggests the presence of rhabdomyolysis in five previously reported cases.[2,7,9] We have documented elevations of serum and urine myoglobin levels in addition, confirming specifically for the first time the presence of rhabdomyolysis and myoglobinuria as part of this syndrome. The precise mechanism of the muscle necrosis in these patients is unclear. Hypotension, fever and substantial hypophosphatemia were present in the case reported herein and may have been pathogenic.[12] Alternatively, a direct effect of the injected material cannot be excluded. In this regard, it is of interest that severe rhabdomyolysis has occurred, in the absence of pressure necrosis, following the intravenous use of adulterated heroin.[13]

The patients' renal insufficiency can be attributed to several factors, including a prerenal component due to volume depletion, acute tubular necrosis due to hypotension and myoglobinuria. In addition, creatine released from injured skeletal muscle cells and spontaneously converted to creatinine may contribute to the elevated levels of the latter in serum of those patients with rhabdomyolysis.[14] In two cases, a low fractional excretion of sodium was found, consistent with prerenal azotemia.[9] Renal function uniformly improved after administering fluid alone, or fluid and mannitol. While the reports are unclear in regard to the duration of renal impairment or the degree of recovery, no patient has required dialysis.

TABLE 1.—*Features of the Intravenous Marijuana Syndrome**

Features	Patients Number	Percent	References
Symptoms			
Myalgia	16	94	1-3,6-9
Nausea, vomiting	16	94	1,2,6-9
Diarrhea	15	88	1,2,6-9
Abdominal pain	11	64	1,2,6-9
Weakness	8	47	1,2,6,7,9
Signs			
Tachycardia	14	82	1-3,6-9
Hypotension (systolic <90 mm of mercury)	14	82	1-3,6-9
Fever (>38.3°C [101°F])	7	41	2,3,6-8
Tachypnea (RR>21)	7	41	2,3,7-9
Muscle tenderness	6	35	2,7,9
Hepatomegaly	4	24	1-3
Altered sensorium	2	12	3,6
Laboratory			
WBC >20,000/μl	14	82	1,2,4,6-9
WBC <4,000/μl	3	18	2,3
Platelets <100,000/μl	8	47	1,2,6,7,9
Azotemia†	14	78	1-3,6-9
↑ CK	6	35	2,7,9
↑ Bilirubin	6	35	1-3,6,7,9
Pulmonary abnormality‡	6	35	1-3,7,9

CK = creatine kinase, RR = respiratory rate, WBC = leukocyte count

*Compiled from data on the patient in this report and 16 cases reported in sufficient detail in the literature. It should be noted that the percentages represent minimum figures because features were assumed to be absent if not mentioned in the reports.
†Creatinine level >1.2 mg/dl or blood urea nitrogen level >21 mg/dl.
‡Abnormalities of chest film, ventilation-perfusion scan or arterial blood gas values.

The thrombocytopenia of this syndrome may be a result of disseminated intravascular coagulation (DIC), which occurs commonly in cases of major rhabdomyolysis.[14] Of five patients with thrombocytopenia who were tested for a partial thromboplastin time, three had prolonged times.[7,9] Further testing of these three patients elicited values for fibrin-degradation products and a prothrombin time consistent with DIC in two cases.[9] Three additional patients have been evaluated by serial assays of factors I, II, V, VII, IX and X. No factor consumption was found, suggesting strongly that DIC was not present.[4] Similarly, when marijuana broth was injected into rabbits, thrombocytopenia ensued in the absence of clotting factor consumption.[4] Thus, the precise role of DIC as a cause of thrombocytopenia in these patients remains unclear; a direct platelet-lowering effect of the injected material remains a possibility.

Pulmonary abnormalities have included mild hemoptysis (n = 1),[1] an elevated alveolar-arterial gradient (n = 1),[2] congestion on chest films (n = 4)[2,3,9] and pleural effusion (n = 1).[9] In the case of one patient with hypoxemia and a diffusely hazy appearance on chest x-ray film, ventilation-perfusion lung scanning showed a nonsegmental variation in blood flow, interpreted as consistent with a diffuse pulmonary vascular process.[9] Capillary leak, pulmonary microvascular embolization of injected particulates and DIC have been suggested as possible mechanisms for the pulmonary abnormalities.[9]

Finally, hyperbilirubinemia and hepatomegaly, found in a few cases, were investigated with a liver biopsy in two. The biopsy specimens showed acute and chronic inflammation, necrosis about the limiting plate, foci of hepatocellular dropout and no foreign bodies. In both cases, liver enzyme values spontaneously improved.[7]

To summarize, in 25 people a reversible multisystem illness developed, characterized by gastrointestinal and myopathic symptoms, tachycardia, hypotension and fever, following the intravenous injection of boiled marijuana preparations. Rhabdomyolysis, renal insufficiency and hematologic, pulmonary and hepatic abnormalities have occurred during the week following IV injection. All patients recovered completely with supportive therapy alone. While selected features of the syndrome may be due to concomitant injection of contaminants or extremely high doses of cannabinoids themselves, the pathogenesis of the IV marijuana syndrome remains unclear.

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Reactivation of Coccidioides Infection

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THE LIST of causes of pulmonary infection in an immunocompromised host is long and continues to grow. Reactivation of prior subclinical coccidioidomycosis is rare. We report two cases of coccidioidomycosis in renal transplant recipients, occurring in a nonendemic area during the hospital stay immediately following transplantation. One patient had coexisting *Pneumocystis carinii* pneumonia.

Reports of Cases

Case 1

The patient, a 40-year-old man, had chronic renal failure due to Alport's syndrome. He was maintained on long-term hemodialysis therapy until he came to San Francisco from Salt Lake City for renal transplantation. He had lived for a few years in Pasadena, California, 20 years before presentation. There was no history of coccidioidomycosis or childhood pneumonia. Results of a pulmonary evaluation including a chest x-ray film were normal on admission to the University of California, San Francisco. He received a living-related donor kidney transplant in late January 1983. Immunosuppression with prednisone (1.5 mg per kg per day) and azathioprine (50 to 150 mg per day) was begun. On the sixth day after transplantation, the prednisone dosage was increased to 3 mg per kg per day, and on the ninth day a six-dose course of antithymocyte globulin was begun for acute transplant rejection. The prednisone dosage was then tapered to 1 mg per kg per day over three weeks.

In the third week of hospital stay, dyspnea on exertion developed. The next day he had cough with minimal hemoptysis and dyspnea at rest. The patient was afebrile with a respiratory rate of 18 breaths per minute. Rales and egophony were noted on chest auscultation. The leukocyte count was 5,400 per μl. Arterial blood gas determinations showed an arterial partial pressure of oxygen of 67 torr, arterial partial pressure of carbon dioxide of 30 torr and pH 7.42. There were diffuse nodular infiltrates on the chest roentgenogram without mediastinal or hilar lymphadenopathy (Figure 1). Sputum evaluation was not revealing. On bronchoscopic examination there were spherules consistent with *Coccidioides immitis* on frozen section examination of the transbronchial biopsy specimens. Culture of these specimens subsequently grew the fungus. The prednisone dosage was reduced to 30 mg per day, azathioprine therapy was discontinued and a course of amphotericin B was begun. A brief period of mechanical ventilation was required for hypoxemia. Sputum cultures became negative for *C immitis* after two months of therapy (2.6 grams of amphotericin B). Chest films showed slow improvement, but at discharge there remained reticulonodular infiltrates. Counterimmunoelectrophoresis for coccidioidomycosis was negative at the onset of infection and at five weeks, but was positive at nine weeks. The complement fixation (CF) titer was less than 1:4 throughout the nine-week period of observation. The patient returned to Utah for follow-up care.

Case 2

The patient, a 35-year-old man with insulin-dependent diabetes mellitus and renal failure, had been receiving hemodialysis for two years before admission. In addition, he had hypertension, diabetic retinopathy and peripheral neuropathy. There was no history of coccidioidomycosis or childhood pneumonia. He lived in Bakersfield, California (endemic for *C immitis*), until age 25 and had been living in San Jose, California (not endemic), since that time.

The patient underwent cadaveric renal transplantation in August 1983, and was placed on a regimen of prednisone, 2.5 mg per kg per day, and azathioprine, 150 mg per day, until the third week after transplantation, when the prednisone dosage was decreased to 1 mg per kg per day and azathioprine

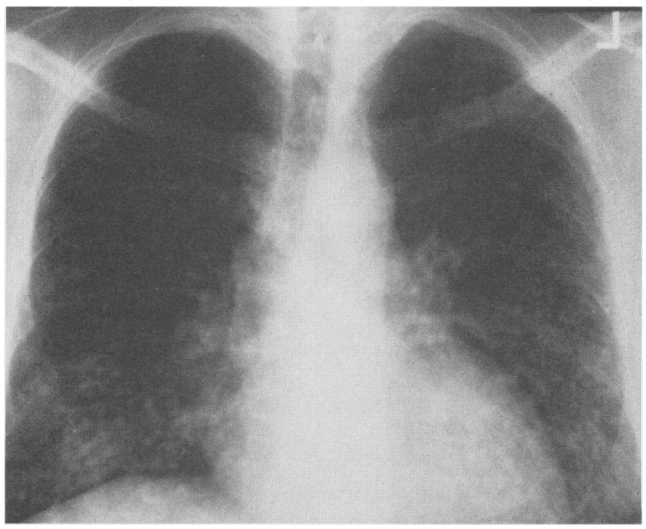

Figure 1.—Chest radiograph of the patient in case 1 showing diffuse nodular infiltrates due to *Coccidioides immitis* infection.

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